Spotting Syphilis: A dual Point-of-Care Syphilis Screening Initiative in a Low-Resource Healthcare Setting

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Protocol Title:	Spotting Syphilis: A dual Point-of-Care Syphilis Screening Initiative in a Low-Resource Healthcare Setting
Principal Investigator:	Irene Stafford MD
Co-Investigators:	Robin Hardwicke MD, Stephen Patrick MD, Sahana Kodali BS, Rachel Hauschel BS, Christina Cortes, MD
Study Coordinator:	If a coordinator / research nurse / research assistant has been identified
Population:	200 women, non-pregnant and pregnant at any gestational age in Puerto Barrios, Guatemala geographic location
Number of Sites:	Single site study in Puerto Barrios, Guatemala
Study Duration:	6 months
Subject Duration:	25 minutes

Background and significance

The Impact of Maternal and Congenital Syphilis

Congenital syphilis results from the transplacental transmission of the sexually transmitted pathogen, Treponema pallidum (T. pallidum) during all trimesters of pregnancy. In addition to significant morbidity of untreated infection to the pregnant woman, the transmission of this highly infectious bacterium results in profound destruction to multiple organ systems in the developing fetus and is associated with a 40% perinatal loss rate, including miscarriage, stillbirth, and neonatal demise1-5

With adult and congenital syphilis rates rising rapidly around the world, it is of critical importance to consider patient-centered approaches to reaching high-risk populations that disproportionately experience syphilis during pregnancy and the tragic outcome of congenital syphilis. Guatemala carries the highest rate of congenital syphilis in Central America with 8.6 per 100,000 neonates infected at birth. There is an urgent need to offer screening with immediate presumptive treatment for maternal syphilis in any heath care setting when a pregnancy is identified in this region. Best practice would include the use of a rapid FDA-cleared point-of-care (POC) test with an opt-out screening strategy for syphilis and HIV testing for all pregnant people presenting to care in high volume pregnancy clinics in Guatemala and is in fact, the WHO recommends dual HIV/syphilis rapid testing as part of antenatal screening, especially in low-resource settings. These meet Inclusion in WHO/PAHO clinical guidance for maternal and public health screening program. Across the globe, opt-out testing for HIV, syphilis and other infections is standard of care during pregnancy, given the high disease burden for neonates of untested and untreated infections during pregnancy. This approach offers routine testing with the option for patients to decline, rather than requiring separate consent for each individual test[4,5]. rapid syphilis and HIV test with immediate results has the advantage of allowing pregnant patients who test positive to be treated on-site, at the same visit, avoiding loss to follow-up and the negative maternal and neonatal consequences associated

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with delayed or missed treatment[2]. Even a single dose of penicillin during pregnancy has demonstrated a reduction in stillbirth[4,5]

Current Diagnostic Challenges in Syphilis and HIV Diagnosis During Pregnancy

'. Lab diagnosis of syphilis can be determined using either the traditional testing algorithm, which screens via a nontreponemal test (eg, rapid plasma reagin [RPR]) followed by a Treponema pallidum–specific assay (eg, T. pallidum particle agglutination assay [TP-PA]); or the reverse algorithm, which uses a treponemal-specific immunoassay (eg enzyme immunoassays (EIAs), and others) followed by reflex nontreponemal test (eg, RPR) for confirmation[4]. An FDA-approved HIV Ag/Ab Combo Assay is used for HIV testing with reflex HIV-1/HIV-2 antibody differentiation[4]. The largest challenge with both tests is the lengthy turnaround time between specimen collection to results reporting. Most labs require days to result a full syphilis and HIV screen with confirmatory results. This lengthy turnaround time from specimen collection to results reporting is a major impediment to syphilis and HIV management, particularly for under resourced communities in Central America. This proposed strategy has the potential to treat maternal syphilis and HIV infection early, and prevent MTCT of HIV and the devastating fetal and neonatal morbidity and mortality of untreated congenital syphilis.

A Novel Approach using a POC test to Detect Syphilis and HIV in Underserved Pregnant Women

We intend to use the Chembio DPP® HIV-Syphilis rapid POC test simultaneously with the current standard opt-out lab-based testing for syphilis and HIV for pregnant women presenting to care using whole blood fingerstick and venipuncture. This test, along with other FDA-approved rapid point-of-care (POC) syphilis tests, is recognized by public health authorities as confirmatory and is used as a reportable result. The Chembio DPP® HIV-Syphilis rapid POC test is included in the WHO list of prequalified in vitro diagnostics (IVDs) and is listed in the Pan American Health Organization (PAHO) Strategic Fund catalog. The positive and negative test agreement (PPA and NPV) for the FDA-approved Chembio DPP® HIV-Syphilis rapid POC compared to routine lab-based tests is excellent, with 95% PPA and > 95% NPV in higher prevalence areas. This has also been demonstrated with the only other FDA-approved syphilis POC test, the Syphilis Health Check, which has demonstrated similar results among 600 patients tested through the Preg-OUT QI program initiated at UTHeath in May, 2023 (PPA 97%, PPV 98%). This program utilizes the opt-out and rapid syphilis testing program for pregnant women presenting to the Hermann ED for care.

Regardless of rapid test results, confirmatory testing will be performed at the same visit by Faith in Practice personnel using a nontreponemal test (RPR) for syphilis and a 4th-generation HIV 1/2 antigen/antibody immunoassay as standard of care for pregnant women. Labs will be batched and sent to Haurte, Guatemala for this purpose. All confirmatory laboratory results will be reported to the Ministry of Health to ensure linkage to appropriate care. Patients will be provided with contact information to the lab to follow results and will be notified by health authorities if syphilis or HIV positive as this is standard car for obstetrics clinics in Los Barrios.

If the POC test is positive for syphilis, empiric intramuscular BPG will be administered according to clinical stage. Additionally, the patient will undergo POC ultrasound for evaluation of fetal congenital syphilis with the investigators. If the HIV test is positive, treatment will be initiated immediately using bictegravir, emtricitabine & tenofovir alafenamide per CDC/WHO recommendations. If lab-based results indicate false positive POC results, patients will be instructed to discontinue treatment. The risks of a false positive are low; however, the patient will be counseled about the small risk of a false positive result which will result in administration of Benzathine penicillin, which in the absence of allergy is unlikely to cause any adverse health effects, outside of pain at injection. If a false positive occurs for HIV, the risk of Bictegravir/Tenofovir Alafenamide (TAF)/Emtricitabine (FTC) administration is also low, which includes nausea. All risks and benefits will be discussed with the patient privately.

this initiative in Guatemala will identify and treat a significant percentage of underserved women who would otherwise not be tested and treated for syphilis and HIV, or are unable to be contacted with positive lab-based positive syphilis or HIV results. *We hypothesize that the utilization of a rapid point-of-care (POC) test for both syphilis and HIV among pregnant patients will increase diagnosis and treatment initiation. We also hypothesize that the use of point-of-care (POC) ultrasound will result in the detection of pregnancies complicated by severe fetal syphilitic infection and will facilitate timely transfers to advanced neonatal centers for indicated specialty care.*

Goals and objectives

Guatemala is experiencing rising rates of sexually transmitted infections (STI), particularly syphilis and HIV. During 2022, the rate of syphilis peaked at 417 cases per 100,000 people. According to UNAIDS data, over 35,000 adults and children in Guatemala are living with HIV, of which over 40% are females of reproductive age. High poverty levels, barriers to healthcare access, and limited testing availability are key drivers of the escalating rates of these STI. **Mother-to-child transmission (MTCT) of syphilis and HIV significantly contributes to neonatal morbidity and mortality, with congenital syphilis being a leading cause of stillbirth in Guatemala and other global communities (WHO, CDC).** With timely detection and treatment, cure is possible, and transmission is preventable[1]. Traditional HIV and syphilis lab-based testing requires advanced lab techniques and turn-around time for results is lengthy. If lab testing is performed in these settings, patients are often unable to follow up or are lost to care. In 2020, the Food and Drug Administration cleared the DPP® HIV-Syphilis test manufactured by Chembio Diagnostic, Inc. as a single-use rapid, qualitative, multiplex, immunoassay for the detection of antibodies to HIV 1 and 2, and/or *T. pallidum* bacteria in fingerstick whole blood, venous whole blood or plasma specimens. With a 15-minute turnaround time and 94.7% sensitivity for syphilis and 99.4% sensitivity for HIV diagnosis, the use of this rapid point of care (POC) test is an ideal method for screening pregnant women living in under resourced settings for syphilis and HIV, where immediate presumptive treatment can be administered or initiated in one visit, reducing the morbidity and mortality associated with congenital syphilis[2]. Point of care ultrasound can also be used to detect in-utero congenital syphilis infection. Traditional ultrasonographic markers for congenital syphilis are profound and include enlarged fetal liver (hepatomegaly), thickened placenta (placentomegaly) and whole-body edema, which can easily be detected by point-of-care ultrasound[3]. Although infected fetuses may not always display these sonographic abnormalities, 87% of fetuses born with congenital syphilis do[3]. Knowledge of these findings prior to delivery can assist providers in facilitating appropriate transfers to higher level of care centers, where these highest-risk neonates can be managed, and life-saving procedures can be performed[4]

Hypothesis

Our study posits that introduction of point of care syphilis and HIV test with diagnostic ultrasound in women in Guatemala will help increase diagnosis, treatments and detection of pregnancies complicated by fetal syphilis among pregnant women there by reducing the devastating effects of MTCT of these infections.

Objectives

Primary

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The objective of this quality intervention study is to determine if a strategy utilizing the Chembio HIV/syphilis rapid POC test for diagnosis of HIV and syphilis in pregnant women attending prenatal clinics in Guatemala will increase screening and detection rates thereby resulting in higher rates of treatment during pregnancy and ultimately reducing congenital syphilis and HIV MTCT. The WHO and global data show that universal screening is not necessarily 100% complaint within the population. This rapid point of care intervention will implement empiric treatment for positive results for patients and their partners and will provide clinical support and provider education on results management and patients will be linked to indicated follow up care.

Secondary

To provide knowledge and technical expertise on the use of Point-of-care ultrasound for all pregnant patients testing positive for syphilis during the intervention to evaluate the fetus for evidence of congenital syphilis. This will include training of the clinicians involved in this project who have knowledge of ultrasound in obstetrics, however will be educated about identification of sonographic evidence of congenital syphilis as published in the Centers For Disease Control and Prevention (CDC) Guidelines and tested on these markers and identification of them before and after the project is completed. Pregnancies with ultrasonographic evidence of fetal congenital syphilis will be referred to a higher level of care for delivery planning and indicated neonatal management.

Outcome measures

Primary

To evaluate if POC HIV/Syphilis test resulted in increased screening, detection and treatment offered to pregnant women with syphilis in Guatemala by the end of the study. Results will be compared to the standard syphilis and HIV testing that will be performed at the same visit, as it is part of routine prenatal care.

Secondary

To assess technical know-how in doctors trained by our team on the use of POC diagnostic ultrasound, in detecting congenital syphilis, by observing their independent use of the equipment and also, to appraise their clinical judgment on appropriate next steps they take after disease confirmation, by referring patients to higher level of care centers by the end of the study. This will be the closest hospital where patients are referred to if there are problems with the fetus or neonate. Elisa Martínez Children's Hospital in Los Barrios, or the Hospital Regional de Escuintla which is the other regional pediatric hospital

Study Design

This is a prospective study using the Chembio HIV/Syphilis rapid POC test for the diagnosis of these prevalent diseases in Guatemala.

The study will last one week with the aim to enroll 200 pregnant women. There may be enrollment of non-pregnant women who present to care for pregnancy concerns and test negative by urine pregnancy test and/or do not have a viable intrauterine pregnancy on ultrasound.

Study aims to increase awareness about these tests to increases testing, speed up diagnosis and reduce loss to follow-up due to lengthy diagnostic process of traditional diagnostic methods.

Also, we aim to equip the doctors with the technical know-how about the use of ultrasound in detecting congenital syphilis per CDC guidelines.

Study Population

Inclusion criteria

Eligible patients (N = 200) will include pregnant women at any gestational age at clinical sites in Puerto Barrios, Guatemala between 09/27/2025 and 10/03/2025.

Nonpregnant women may also be included if unsure of pregnancy status and attend clinic for pregnancy care and confirmed to be not pregnant by routine testing such as urine pregnancy tests and/or the absence of an intrauterine pregnancy by ultrasound .

Exclusion criteria

Participants who do not meet inclusion criteria

Study Procedures

- Between 09/27/2025 and 10/03/2025, all pregnant women and otherwise confirmed non-pregnant women presenting for pregnancy care at the Los Barrios Health clinic established by Guatemala-based Faith in Practice providers will be tested for syphilis and HIV per standard of care with the lab-based testing methods by the providers in clinic. This includes the nontreponemal tests for syphilis (RPR) and the 4th generation HIV-1/2 antigen/antibody immunoassay. The health team in Los Barrios will complete all lab-based HIV and syphilis testing and will batch send to Huarte, Guatemala.
- The patient will also undergo the Chembio DPP® HIV-Syphilis rapid POC test by fingerstick during the same visit in a private exam room by the study team according to the protocol for this quality health initiative.
- The Chembio test is read by a handheld reader. If positive for syphilis, the patient will be informed and treated at the same visit with IM Benzathine penicillin G (BPG) according to clinical stage[4,5]. It is expected that of the 200 patients only a percentage will be positive and of those 50% are expected to be at stage 1 and will require 1 dose. The remainder of the positives will need a 3 weeks supply, which will be provided to them.
- If positive for HIV, she will be started on Bictegravir/Tenofovir Alafenamide (TAF)/Emtricitabine (FTC) per guidelines[4,5]. Medications will be paid for by grant funds for initiation of treatment only and further indicated doses will be managed by the Ministry of Health.
- Partners will be offered empiric treatment if not penicillin allergic in accordance with public health guidelines. Patients positive for syphilis by the POC will undergo point-of-care ultrasound for the detection of fetal markers for congenital syphilis by the study team and recorded.
- If any one of the following sonographic markers are present at any gestational age (GA) > 34 weeks; hydrops, placentomegaly or hepatomegaly (> 95% for GA)[3], delivery planning and referral to a higher level-facility will be initiated for indicated neonatal management.
- Patients will be asked to follow up with the lab for results after the visit according to the standard care at this health center. Information and instructions will be given to the patient so she may follow up results before she is discharged from the clinic. All positive results are reportable to the Health Ministry in Guatemala who manage HIV and further syphilis care.The study team will record all data using an institutional protected cloud based database RedCAP.

Statistics

Data Analysis Plan:

Descriptive statistics will summarize the study population. Frequency tables will report the number of patients approached, tested using the Chembio DPP® HIV-Syphilis point-of-care (POC) test, and those tested with laboratory-based methods.

Participant demographics will include age, race/ethnicity, preferred language, marital status, education level, and health insurance status. Obstetric history will include gravidity, parity, number

of pregnancy losses, history of preterm birth, cesarean delivery, and gestational age at testing. Prior STI diagnoses and treatments will also be reported.

Ultrasound findings (e.g., placentomegaly, hepatomegaly, echogenic bowel, fetal growth restriction, abnormal femur length) will be summarized using mean (standard deviation) for continuous variables and N (%) for categorical variables. Each finding will be evaluated for its frequency and consistency with known sonographic indicators of congenital syphilis.

Provider training outcomes will include pre- and post-training quiz scores, analyzed using paired t-tests or Wilcoxon signed-rank tests. Quiz item-level performance will identify content areas of greater or lesser understanding. Image acquisition and visualization success will be evaluated using standardized scoring tools and summarized by frequency. McNemar's test or Cochran's Q test will assess changes in the proportion of successful image acquisition over time.

Where appropriate, subgroup comparisons (e.g., visualization of specific ultrasound findings by patient gestational age or provider experience) will be analyzed using chi-square tests for categorical variables and t-tests or ANOVA for continuous variables.

All statistical analyses will be conducted using Stata 17. A significance level of $p < 0.05$ will be used for all hypothesis testing.

Ethics

IRB approval will be sort before the commencement of this study

We will also be requiring a waiver of documentation of consent as participants will be undergoing routine pregnancy care. Part of routine pregnancy care is screening for HIV and syphilis. In fact, in global communities, WHO recommends dual HIV/syphilis rapid POC testing as part of routine antenatal screening. As this is standard of care to screen for these infections and perform fetal ultrasound for congenital syphilis in pregnant women with syphilis, we are requesting a waiver of documentation of informed consent. All labs, including type and screen, viral hepatitis and more are performed in pregnancy using an opt-out strategy that is explained in the general consents. Therefore, we are not performing any non-routine tests. Ultrasound is also standard of care and will be described in the general consent for care.

Patients will be provided with information about the study and asked verbally if they will like to part of the study and tested. Because the study will be explained to each patient and all of the testing is part of SOC for pregnancy, we believe the waiver of documentation of consent will not adversely affect their rights and poses no more than minimal risk.

Timeline

All proposed study initiation steps will be performed 06/24-07/26.

Institutional Review Board approval will occur between 06/25 – 08/25.

Purchase of medicine and ultrasound machines 07/25 – 08/25.

Proposed travel and work dates 09/27/25 – 10/04/25.

Training 09/27/25 and completion with wrap up 10/04/25.

Data analysis and completion of presentation and manuscript drafts 12/25 – 02/26.

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Data handling and record keeping

All data will be recorded in the institutional secured cloud-based database RedCAP by the team after enrollment.

This will include all demographic and obstetrical data, POC and lab-based testing results and treatment regimens as described in the Statistics section

Quality control and assurance

The PI and co-investigators will go through all the files to assure the data is reliable and complete. The verification will be by self-assessment.

Impact Statement

If this study demonstrates that opt-out and rapid HIV and syphilis testing improves treatment initiation for syphilis and may improve antiviral therapy initiation for pregnant women with HIV, health agencies may support this screening and treatment method for of all pregnant women presenting to care in non-traditional settings, reducing the health disparities surrounding perinatal syphilis and HIV.

Research Team

Our investigative team includes;

Dr. Irene Stafford (PI), a maternal-fetal medicine specialist at UTHealth with expertise in congenital syphilis.

Dr. Robin Hardwicke (Co-I), an internal medicine provider at UTHealth specializing in pregnant patients with HIV.

Dr. Stephen Patrick (Co-I), the residency director of UT Tyler Ob/Gyn with over 15 years of global health experience.

Dr. Christina Cortes, an Obstetrics and Gynecology resident at UTHealth with an interest in congenital infections.

Rachel Hauschel , a second year medical student at UTHealth with an interest in congenital infections and a global health concentration.

Sahana Kodali, a second-year medical student with a global health concentration.